ABSTRACT OF THE DISCLOSURE

A novel gene therapy for cancer has been discovered, which unlike most prior approaches, does not require specific knowledge of the cancer cells, but instead targets a general characteristic that distinguishes cancer cells from normal cells, i.e., elevated eIF4E expression. The expression of a toxin or conditional toxin such as HTK is translationally repressed in normal cells by placing a complex 5' UTR in front of its reading frame. In prototype experiments, this HTK mRNA, a transcriptional product of the BK-UTK vector, was translationally regulated so as to largely inhibit its production in normal murine and human cells, while cancer cells efficiently translated the protein, which a resulting increased sensitivity to GCV. Synthesis of the HTK protein from the BK-UTK vector (containing the 5' UTR of Fibroblast growth factor - 2 ("FGF-2") readily occurred in a panel of murine and human breast carcinoma lines, but not in normal cell lines. Subcutaneous tumors and experimental lung metastases of the breast carcinoma line MM2MT in BALB/c mice were greatly reduced by transfection with the BK-UTK vector, followed by GCV administration. Both the BK-UTK and the BK-TK (control) vectors were effective in reducing lung metastasis following systemic delivery of the vectors and subsequent GCV administration. However, the BK-TK vector was highly toxic to mice while little to no toxicity was seen in mice treated with the BK-UTK vector.